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| 10/661,939 | 09/12/2003 | Frank A. Skraly | MBX 048 | 8379 |

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| EXAMINER |
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| CHOWDHURY, IQBAL HOSSAIN |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1652 | |

DATE MAILED: 11/29/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/661,939 | SKRALY, FRANK A. | |
| | Examiner | Art Unit | |
| | Iqbal H. Chowdhury, Ph.D. | 1652 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *08 September 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *16-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Application Status*

Claims 1-12, 16-35 are currently pending in this office action. Claims 16-23 are now under consideration. Claims 1-12 and 24-35 remain withdrawn being drawn to non-elected invention.

Applicants' amendments and arguments filed on September 18, 2006, have been fully considered but are not deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

The examiner acknowledges the submission of sequence listing and amendment to the claims.

Previous rejections of Claims 16 and 23 under 35 U.S.C. 102(b) and Claims 16-23 under 35 U.S.C. 103(a) are withdrawn in view of applicants amendment of claims and persuasive arguments.

### *Maintained-Claim Rejections - 35 USC § 112*

Previous rejection of Claims 16-23 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed,

had possession of the claimed invention. This rejection has been described in length in previous Office Actions. Applicant's amendments and arguments have been fully considered but are not deemed persuasive for the following reasons.

Applicants argue that the examiner is confused with the claimed invention that is an organism and method of use of said organism wherein said organism is transformed with known genes in a new combination and that the claims are not drawn to new genes or a new genus of enzymes and the individual components of the claimed combinations and methods of use are all known, and readily available. Applicants also argue that it is well established that in such cases it is more than adequate to provide representative sources for materials, so long as the selection criteria and instructions on how the materials are to be used are clearly taught by applicants. Applicants further argue that from the thorough description in the specification, it is clear that the Applicants were in possession of the claimed subject matter and that CoA-dependent dehydrogenase is well known in the art, and the specification (from page 9, line 13, to page 10, line 8), describes different organisms that can serve as sources for CoA-dehydrogenase. Applicants' also refer to the GenBank accession numbers as a source for the sequences of known CoA-dependent aldehyde dehydrogenases in various species (page 10, lines 27-30) and argue that genes involved in PHA synthesis as well as their sources are also known in the art (page 3, lines 9-12 of the specification).

In summary, applicants argue that a patent need not teach, and preferably omits, what is well known in the art.

Applicant's arguments have been fully considered but are not deemed persuasive to overcome the rejection of claims 16-23. The examiner acknowledges the amendment to the

claims and references but disagrees with the applicant's contention that the claimed invention is adequately described. Claims 16-23 is directed to a recombinant organism comprising and expressing a heterologous gene encoding any CoA-dependent aldehyde dehydrogenase and any PHA synthase from any source for producing polyhydroxyalkanoates (PHAs).

While applicants' argue that claims are not drawn to genes or enzymes but directed to microorganisms and that Examiner has confused the invention, claims rejected are indeed drawn to microorganisms comprising said enzymes whose structure is not disclosed. Examiner respectfully disagrees with the applicants' that the invention has been confused. In order to satisfy Written Description requirement, Applicants are required to disclose adequate description of the specific structural feature of the genus (genes) used to make the organism; such that one of the ordinary skill in the art can easily practice the claimed invention. If the genus (genes) of polynucleotides expressing the enzymes is not described adequately, then organisms comprising the same are also not described.

In addition, the microorganisms used in the method comprising the genus of any CoA-dependent aldehyde dehydrogenase and any PHA synthase is a very large genus having different structures. In the instant case claim 16 reads on a microorganism comprising any CoA-dependent aldehyde dehydrogenase and any PHA synthase i.e. there is no structural feature, which is representative of all the members of the heterologous CoA-dependent aldehyde dehydrogenase and PHA synthase recited in the claim. Many variants and mutant polypeptides with varied structure are encompassed by the recited genus. The specification teaches the structure of a single CoA-dependent aldehyde dehydrogenase isolated from E. coli and the structure of a single PHA synthase isolated from Aeromonas caviae, having the respective functional characteristics,

which is insufficient to adequately describe the structure of required genus of heterologous CoA-dependent aldehyde dehydrogenase and PHA synthase having recited functional characteristics. Therefore. One ordinary skill in the art will not be able to conclude that applicants' were in possession of the claimed invention. Therefore, the rejection is maintained.

Previous rejection of Claims 16-23 under 35 U.S.C. 112, first paragraph, because the specification while being enabling for recombinant E. coli DH5α comprising a plasmid expressing the CoA-dependent aldehyde dehydrogenase gene eutE from E. coli and PHA synthase from Aeromonas caviae, does not reasonably provide enablement for a recombinant organism comprising a plasmid having any CoA-dependent aldehyde dehydrogenase gene or any PHA synthase gene or any acyl-CoA transferase gene from any source. This rejection has been discussed at length in the previous office action. It is maintained for the reasons of record and discussed below.

With respect to the claims 16-23 the applicants argue that genetically engineered plants and bacteria that make polyhydroxyalkanoates are known, having been described in the patent literature and the problem applicants were addressing is how to produce recombinant organisms that can produce high levels of medium chain length polyhydroxyalkanoates (page 3, line 27 to page 4, line 3 and page 8, lines 27-30) while avoiding increasing the level of 3-hydroxyacid in the feed, avoiding the use of 3-propionic acid in the feed, and avoiding the generation of free propionic acid in the cytosol. Applicants also argue that the solution, as described on page 4, lines 5-15, page 8, line 27 to page 9, line 12, and defined by the claims, is to provide, in addition to the other enzymes for polyhydroxyalkanoate production (beta-ketothiolase, acetyl CoA

reductase and PHA synthase, all of which are known), a CoA aldehyde dehydrogenase which directly converts any aldehydes generated from the alcohols used as co-feed, into the corresponding acyl-CoA. Applicants' further argue that the claims define a recombinant organism for producing polyhydroxyalkanoate, comprising a heterologous gene encoding a CoA-dependent aldehyde dehydrogenase and a PHA synthase. Furthermore, applicants argue that the specification (from page 9, line 13, until page 10, line 8) extensively describes different organisms that can serve as sources for CoA-dehydrogenase, providing gene bank accession numbers and a source for the sequences of known CoA-dependent aldehyde dehydrogenases in various species (see page 10, lines 27-30) and techniques for developing recombinant PHA producers are known in the art (see Madison). Applicants maintain that once a gene is identified, it is routine in the art to incorporate the gene into a plasmid, or the chromosome, for expression in the cells. Applicants argue that there is sufficient guidance in the specification to construct plasmids and express the claimed genes and the experimental protocols are routine and expression vectors, restriction enzymes and ligation enzymes are commercially available. Although there is no need for examples, Applicants submit that they have provided examples to show that one can isolate, identify and express the enzymes in organisms as recited in the claims and that based on the teachings in the specification, and the state of the art, one of ordinary skill in the art would be able to make a recombinant organism as claimed.

Applicant's arguments have been fully considered but are not deemed persuasive to overcome the rejection of claims 16-23. The examiner acknowledges the amendment to the claims 16 and 17 and references but disagrees with the applicant's contention that the claimed invention is enabled for full scope claimed.

The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the microorganism comprising extremely large number of aldehyde dehydrogenase gene (CoA-dependent), PHA synthase gene or acyl-CoA transferase gene broadly encompassed by the claims. The claims read on as organisms comprising mutants, variants or recombinants of any aldehyde dehydrogenase gene (CoA-dependent), any PHA synthase gene or acyl-CoA transferase gene. The disclosure is limited to a microorganism comprising the nucleotide and encoded amino acid sequences of only one aldehyde dehydrogenase gene (CoA-dependent), one acyl-CoA transferase gene or one acyl-CoA synthetase or one β-ketothiolase and one acetoacetyl-CoA reductase gene and three PHA synthase gene. Applicants have not, first of all provided a method of making all of the variants mutants of the E. coli CoA-dependent aldehyde dehydrogenase and PHA synthase. Second, they have not shown that any of the variants and mutants or recombinants of the above enzyme would successfully work in any organism including any bacteria, fungi, yeast, plant or animal to produce these enzymes. Without specific guidance, one of the of the ordinary skill in the art would have to test each and every one of aldehyde dehydrogenase gene (CoA-dependent), PHA synthase gene or acyl-CoA transferase gene to make a recombinant organism and test the same for producing polyhydroxyalkanoates (PHAs). Therefore, one of the ordinary skilled in the art would be subjected to undue experimentation to make and use the claimed invention.

As argued in the rejection, the specification fails to support the broad scope of the claims that encompass any recombinant organism including recombinant bacteria or recombinant plant comprising a plasmid having any aldehyde dehydrogenase gene (CoA-dependent), any PHA synthase gene or any acyl-CoA transferase gene because the specification does **not** establish: (A)

regions of the protein structure which may be modified without effecting polypeptide activity; (B) the general tolerance of polypeptide to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any CoA-dependent any aldehyde dehydrogenase or any acyl-CoA transferase or PHA synthase residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any recombinant organism or any recombinant bacteria or any recombinant plant comprising a plasmid having any CoA-dependent aldehyde dehydrogenase gene or any PHA synthase gene or any acyl-CoA transferase gene. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, making a recombinant organism comprising a plasmid expressing any of said genes having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). Therefore, for the reasons above, the rejection is maintained.

***Conclusion***

No claims are in condition for allowance. Applicants must respond to the objections/rejections in each section in this Office action to be fully responsive in prosecution.

**THIS ACTION IS MADE FINAL.** See M.P.E.P. § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. § 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Iqbal Chowdhury, Ph.D. whose telephone number is 571-272-8137. The examiner can normally be reached on 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 703-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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